Complete Summary

GUIDELINE TITLE

Venous thromboembolism (VTE).

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Venous thromboembolism (VTE). Ann Arbor (MI): University of Michigan Health System; 2004 Aug. 11 p. [5 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. Venous thromboembolism (VTE). Ann Arbor (MI): University of Michigan Health System; 1998. 10 p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Venous thromboembolic disease (VTE), comprised of:

- Deep venous thrombosis (DVT), and
- Pulmonary embolism (PE)

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Family Practice
Hematology
Internal Medicine
Neurology
Obstetrics and Gynecology
Oncology
Orthopedic Surgery
Pharmacology
Pulmonary Medicine
Radiation Oncology
Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Pharmacists
Physicians

GUIDELINE OBJECTIVE(S)

- To improve the recognition of venous thromboembolism (VTE) and selection of appropriate testing for VTE
- To shorten resolution time for clinical symptoms
- To reduce incidence of pulmonary embolism
- To reduce mortality
- To reduce bleeding complications
- To reduce costs of hospitalization and occurrence of complications

TARGET POPULATION

Adults with suspected acute deep venous thrombosis of the lower extremity, pulmonary embolus, or both

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Diagnosis of deep venous thrombosis (DVT)
    - Clinical likelihood estimation
    - Venous color duplex Doppler ultrasound imaging
    - D-dimer assays (for exclusion in low-probability patients only)
    - Phlebography (seldom indicated)
2. Diagnosis of pulmonary embolism (PE)
    - Clinical likelihood estimation
    - Ventilation-perfusion (V/Q) scanning

- Venous color duplex Doppler ultrasound
- D-dimer assays (with formal clinical likelihood estimation to exclude low-probability patients only)
- Pulmonary angiography
- Helical computer tomography (CT) (to establish but not to rule out PE)
- Magnetic resonance imaging (MRI) angiography (not recommended)

Treatment

1. Heparin anticoagulation
    - Heparin followed by warfarin
    - Low molecular weight heparin (LMWH)
    - Unfractionated heparin (UFH)
    - Outpatient treatment
    - Aggressive treatment (thrombolytic therapy with tissue-type plasminogen activator [t-PA] in exceptional cases only)
2. Warfarin (Coumadin) anticoagulation
3. Inferior vena cava filters, if anticoagulation is contraindicated or has failed
4. New non-heparin anticoagulant agents (e.g., lepirudin, agratroban)

Monitoring

1. Low molecular weight heparin (LMWH): monitoring of platelet counts to identify heparin-induced thrombocytopenia
2. Unfractionated heparin (UFH): activated partial thromboplastin time (APTT); thrombin time (also referred to as the thrombin clotting time or TCT); daily platelet counts
3. Warfarin therapy: prothrombin time (PT) and international normalized ratio (INR), home INR monitoring, and testing for thrombophilia (in those with recurrent venous thromboembolism [VTE] or family history only)

MAJOR OUTCOMES CONSIDERED

- Duration of clinical symptoms
- Length of hospital stay
- Recurrence rate of thrombosis (pulmonary embolism [PE] or deep vein thrombosis [DVT])
- Incidence of pulmonary embolism
- Mortality and complication rates
- Incidence of bleeding complications

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The initial prospective literature searches for this project were performed in 1996 and 1997. The current update is based on a supplemental literature search

performed in December 2002 for literature published since the initial searches. The population was adults. Major key words were pulmonary embolism and deep venous thrombosis thrombophlebitis (includes venous thromboembolism, thromboembolism, venous thrombosis). Additional search terms were duplex venous scan, pulmonary angiography, ventilation perfusion (V/Q) scan, arterial blood gasses (O2 saturation), computed tomography, D-dimer, recurrent pulmonary embolism, pulmonary hypertension – embolism, pregnancy, low molecular weight heparin, heparin, warfarin, international normalized ratio, prothrombin time, vena cava filter, temporary filter, massive pulmonary embolism, failure of therapy, diagnosis, therapy, clinical trials, and guidelines. Detailed search terms and strategy are available upon request.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence for the Most Significant Recommendations

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Quantitative consideration of benefits, harms, costs, and patient preferences

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

UMHS guidelines are reviewed by leadership and in clinical conferences of departments to which the content is most relevant. Guidelines are approved by the Primary Care Executive Committee (PCEC) and the Executive Committee of Clinical Affairs (ECCA).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the full-text guideline for additional information, including detailed information on dosing recommendations (i.e., a body weight-based intravenous heparin dosing nomogram) and test performance characteristics of V/Q scanning.

The levels of evidence [A-D] are defined at the end of the Major Recommendations.

Initiate Treatment Immediately

Patients without contraindications to heparin should begin full-dose heparinization at once [A]. If pulmonary embolism (PE) is clinically likely, initiation should not await testing; if only deep vein thrombosis (DVT) is suspected and testing will be prompt, initiation may await testing. Therapeutic levels of anticoagulation should be achieved as quickly as possible. Warfarin should be initiated on day 1 of treatment, after heparin loading is complete.

Diagnosis

- Deep Venous Thrombosis
    - Clinical likelihood estimation. Symptoms and signs alone are not adequately sensitive or specific for diagnosis or exclusion of venous

thromboembolism (VTE), but clinical likelihood estimation based on symptoms and signs is a necessary step in the testing strategy.
    - Lower extremity DVT: Venous color duplex Doppler ultrasound imaging is the standard for diagnosis [A]. Depending on the clinical likelihood estimate, high-sensitivity D-dimer testing can exclude DVT without imaging (see the original guideline document for more information).
- Pulmonary Embolism
    - Lab tests inadequate. D-dimer testing without other information or blood gas determination is not adequately sensitive or specific to diagnose or exclude PE.
    - Clinical likelihood estimation + ventilation-perfusion (V/Q) scan. Diagnosis requires clinical likelihood estimation plus V/Q scanning. Under certain clinical conditions PE can be diagnosed or excluded without V/Q scanning (see the original guideline document for more information).
    - Pulmonary angiography. Perform when the clinical likelihood estimate yields a reasonable likelihood of PE, but V/Q results are low or intermediate probability, lower extremity Doppler studies are negative, and the risk of complications of treatment is high.

Treatment

- Heparin
    - Low molecular weight heparin (LMWH) preferred. LMWH is preferred over unfractionated heparin (UFH) for both safety and cost reasons [A].
    - Outpatient use of LMWH for DVT. LMWH is appropriate for most patients with DVT to use at home. Some require initial brief hospital admission and stabilization; clinically stable low-risk patients can initiate treatment in the outpatient setting using LMWH.
    - Unfractionated heparin. If UFH is used, it should be initiated and dosed in a structured manner to achieve therapeutic levels rapidly with minimal adjustment [A].
    - Minimum time period. Heparin (LMWH or UFH) must be continued for at least five days in order to minimize the risk of extension of thrombosis or occurrence or recurrence of embolism [B].
    - If heparin contraindicated. Patients who are not candidates for heparin anticoagulation due to risk of major bleeding or to drug sensitivity (heparin-induced thrombocytopenia [HIT]) may be candidates for one of the new non-heparin anticoagulant agents (e.g., lepirudin, agratroban). Those who cannot use any anticoagulant should have an inferior vena cava filter placed to prevent pulmonary embolization [B*].
- Warfarin. Patients should begin warfarin on day one of heparin therapy after heparin loading is complete, and international normalized ratios (INRs) must be >2.0 before discontinuation of heparin [A, B]. Start warfarin at the anticipated therapeutic dose; loading doses are no longer considered appropriate.
    - If warfarin contraindicated. Patients who can receive heparin but cannot take warfarin (e.g., during pregnancy) may be anticoagulated

for several months with full-dose subcutaneous heparin [A], preferably LMWH.

- Aggressive therapy. Patients with extensive proximal DVT producing severe limb swelling and pain, or patients with massive PE producing shock or systemic hypoperfusion may be candidates for emergent thrombolytic therapy or (in the case of DVT) thrombectomy. Such patients should be discussed with a consultant immediately.

Definitions:

Levels of Evidence for the Most Significant Recommendations

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational analysis
D. Opinion of expert panel

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for the diagnosis of pulmonary embolism.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is identified and graded for the most significant recommendations (see "Major Recommendations").

Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials (RCTs) were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis, treatment, and management of venous thromboembolism

POTENTIAL HARMS

- Complications of anticoagulation therapy include major bleeding, heparin-induced thrombocytopenia (HIT), and warfarin-induced skin necrosis.
- HIT is an uncommon but serious complication of heparin therapy that can cause arterial and venous thrombosis, and less often bleeding.
- Phlebography carries appreciable local morbidity, the risk of contrast administration, and is technically inadequate in 7 to 20% of studies.

- The use of inferior vena cava (IVC) filters may result in the following complications: deep venous thrombosis (DVT) at insertion site; change in filter position (tilting, migration); perforation of inferior vena cava; IVC thrombosis; local trauma to skin, vessels, and nerves at insertion site.

  Some medications (aspirin or any aspirin-containing products; Vitamins C, K, E, or other high-potency vitamins; laxatives; and antacids) can interact and/or interfere with warfarin causing serious side effects.

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications to anticoagulation include fresh surgical wound; active gastrointestinal (GI) or other bleeding (not occult blood); recent hemorrhagic cerebrovascular accident (CVA); multiple/major trauma; recent neurosurgery; and inability or unwillingness to comply with oral anticoagulation.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Jun (revised 2004 Aug)

GUIDELINE DEVELOPER(S)

University of Michigan Health System - Academic Institution

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Internal funding for University of Michigan Health System guidelines is provided by the Office of Clinical Affairs. No external funds are used.

GUIDELINE COMMITTEE

Venous Thromboembolism Guideline Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the University of Michigan Health System Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 20, 1999. The information was verified by the guideline developer on June 17, 1999. This NGC summary was updated on November 8, 2004. The updated information was verified by the guideline developer on December 7, 2004.

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